Mechanical and oral antibiotic bowel preparation versus no bowel preparation for elective colectomy (MOBILE): a multicentre, randomised, parallel, single-blinded trial

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Summary

Background Decreased surgical site infections (SSIs) and morbidity have been reported with mechanical and oral antibiotic bowel preparation (MOABP) compared with no bowel preparation (NBP) in colonic surgery. Several societies have recommended routine use of MOABP in patients undergoing colon resection on the basis of these data. Our aim was to investigate this recommendation in a prospective randomised context.

Methods In this multicentre, parallel, single-blinded trial, patients undergoing colon resection were randomly assigned (1:1) to either MOABP or NBP in four hospitals in Finland, using a web-based randomisation technique. Randomly varying block sizes (four, six, and eight) were used for randomisation, and stratification was done according to centre. The recruiters, treating physicians, operating surgeons, data collectors, and analysts were masked to the allocated treatment. Key exclusion criteria were need for emergency surgery; bowel obstruction; colonoscopy planned during surgery; allergy to polyethylene glycol, neomycin, or metronidazole; and age younger than 18 years or older than 95 years. Study nurses opened numbered opaque envelopes containing the patient allocated group, and instructed the patients according to the allocation group to either prepare the bowel, or not prepare the bowel. Patients allocated to MOABP prepared their bowel by drinking 2 L of polyethylene glycol and 1 L of clear fluid before 6 pm on the day before surgery and took 2 g of neomycin orally at 7 pm and 2 g of metronidazole orally at 11 pm the day before surgery. The primary outcome was SSI within 30 days after surgery, analysed in the modified intention-to-treat population (all patients who were randomly allocated to and underwent elective colon resection with an anastomosis) along with safety analyses. The trial is registered with ClinicalTrials.gov, NCT02652637, and EudraCT, 2015–004559–38, and is closed to new participants.

Findings Between March 17, 2016, and Aug 20, 2018, 738 patients were assessed for eligibility. Of the 417 patients who were randomised (209 to MOABP and 208 to NBP), 13 in the MOABP group and eight in the NBP were excluded before undergoing colonic resection; therefore, the modified intention-to-treat analysis included 396 patients (196 for MOABP and 200 for NBP). SSI was detected in 13 (7%) of 196 patients randomised to MOABP, and in 21 (11%) of 200 patients randomised to NBP (odds ratio 1·65, 95% CI 0·80–3·40; p=0·17). Anastomotic dehiscence was reported in 7 (4%) of 196 patients in the MOABP group and in 8 (4%) of 200 in the NBP group, and reoperations were necessary in 16 (8%) of 196 compared with 13 (7%) of 200 patients. Two patients died in the NBP group and none in the MOABP group within 30 days.

Interpretation MOABP does not reduce SSIs or the overall morbidity of colon surgery compared with NBP. We therefore propose that the current recommendations of using MOABP for colectomies to reduce SSIs or morbidity should be reconsidered.

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Introduction

Although postoperative recovery of colon surgery has improved over the past few decades because of minimally invasive techniques and enhanced recovery after surgery (ERAS) protocols,[1,2] colon surgery is still associated with morbidity. The majority of morbidities arise from surgical site infections (SSIs),[3–4] which can vary from superficial wound infections to life-threatening colonic anastomotic leakage. Mechanical bowel preparation was once routinely used and thought to improve outcomes; however, it has not been recommended for nearly two decades because evidence from randomised trials, and later meta-analyses and a Cochrane review, indicated no benefit over no bowel preparation (NBP) in elective colon surgery.[5–8]

Results from several large retrospective series stemming from the American College of Surgeons National Surgical Quality Improvement Program (ASC NSQIP) have challenged the dogma surrounding NBP and suggested that mechanical and oral antibiotic bowel preparation

Research in context

Evidence before this study

Bowel preparation for elective colectomies has not been routinely used during the past few decades. Results of several large retrospective series stemming from the American College of Surgeons National Surgical Quality Improvement Program have suggested that mechanical and oral antibiotic bowel preparation (MOABP) decreases the rate of surgical site infections (SSIs) and overall complications compared with no bowel preparation (NBP). Before initiation of the study trial in November, 2015, we searched PubMed and ClinicalTrials.gov for randomised clinical trials published in English, between January, 1980, and November, 2015, that had compared MOABP with NBP using the search terms "bowel preparation and colon", "colectomy", or "colorectal". We did not find any randomised controlled trials.

Added value of this study

This is, to our knowledge, the first randomised trial comparing MOABP with NBP before colectomy. The primary outcome, SSI, was similar between the MOABP and NBP groups (7% *vs* 11%). Furthermore, the total burden of complications, measured using Comprehensive Complication Index, did not differ between the groups (10·0 points in the MOABP group, 9·0 points in the NBP group) and anastomotic dehiscence (4% *vs* 4%), reoperations (8% *vs* 7%), or hospital stay (5·4 days for MOABP and 5·3 days for NBP) were also similar between the groups.

Implications of all the available evidence

Our study proposes to reconsider the current recommendations of using MOABP for colectomies to reduce SSIs or morbidity.

(MOABP) decreases the rate of SSIs and overall complications compared with NBP.[9–16] Four large societies have changed their recommendations on the basis of these large retrospective trials. The American Society of Colon and Rectal Surgeons, the Society of American Gastrointestinal and Endoscopic Surgeons, the American Society for Enhanced Recovery, and the Perioperative Quality Initiative all now recommend MOABP over NPB.[17–19] Notably, no prospective randomised trials have yet compared MOABP with the current standard of care, which is NBP. A meta-analysis[20] also emphasised the scarcity of literature on the comparison between MOABP and NBP. Although many randomised controlled trials have compared MOABP with mechanical bowel preparation, and show benefit in favour of MOABP,[20–23] the results cannot be extrapolated to the NBP strategy. Mechanical bowel preparation could increase the prevalence of SSIs, for reasons that remain unknown.[24]

Because of scarcity of evidence and controversy regarding the benefits of MOABP, we did a study to compare MOABP with NBP for elective colectomy (the MOBILE trial). Our hypothesis, based on retrospective series, was that MOABP reduces the prevalence of SSIs and overall complications following colon surgery. We report here the primary and secondary outcomes; tertiary and long-term survival outcomes will be reported at the 5-year follow-up.

Methods

Study design

The MOBILE trial was a national, multicentre, single-blinded, parallel group, individually randomised superiority trial comparing MOABP with NBP in patients undergoing elective colon surgery. The trial was done in four Finnish hospitals: two university hospitals (Helsinki University Hospital and Oulu University hospital) and two community (central) hospitals (Central Finland Central Hospital and Seinäjoki Central Hospital). All participating hospitals are government funded and provide care to all patients within their catchment area. Colonic surgery is extremely rare in private hospitals in Finland. The research plan was approved by the Finnish National Committee on Medical Research Ethics and Finnish Medicines Agency. The research plan was

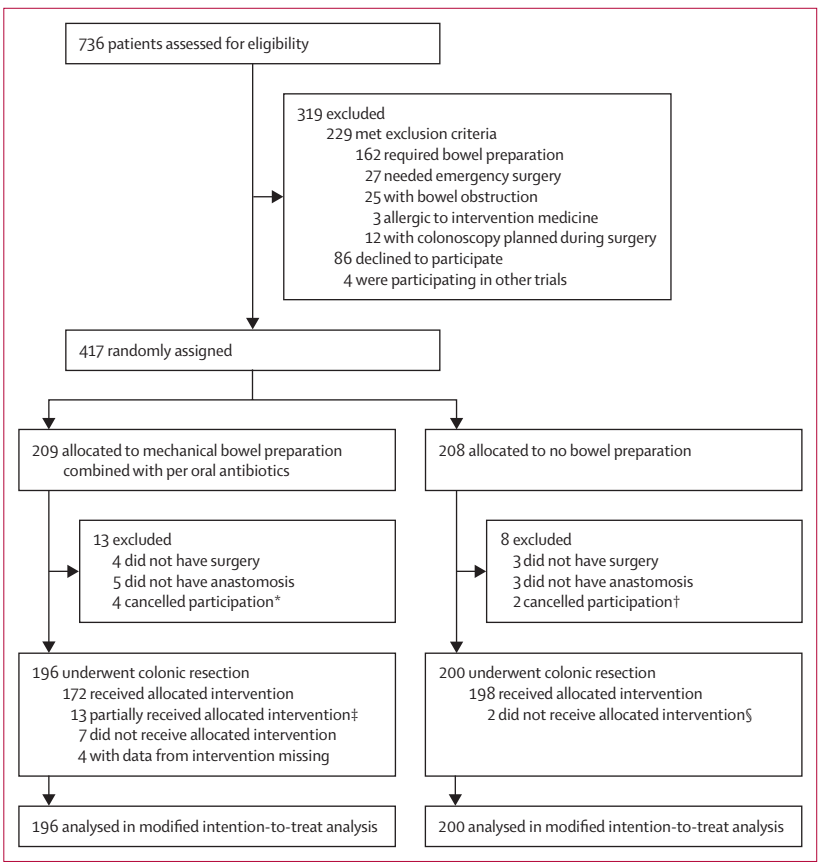

Figure: **Trial profile**

*One patient required emergency surgery and three patients withdrew consent. †One patient underwent operation in another hospital and one patient withdrew consent. ‡Eight patients only partially prepared their bowel with polyethylene glycol, one took antibiotics before bowel preparation, three only partially received antibiotics, and one did not take antibiotics. §Two patients prepared bowel with polyethylene glycol.

	Mechanical and oral antibiotic bowel preparation (n=196)	No bowel preparation (n=200)
Demographics		
Age, years	69·9 (61·1–75·2)	70·3 (61·0–76·0)
Sex		
Female	91 (46%)	104 (52%)
Male	105 (54%)	96 (48%)
Body-mass index, kg/m²	27·0 (4·3)*	27·2 (5·2)
Albumin concentration, g/L	36·4 (5·2)†	35·7 (4·6)‡
Smokers	19/190 (10%)§	16/191 (8%)¶
ASA physical status score		
1	20 (10%)	23 (12%)
2	77 (39%)	85 (43%)
3	88 (45%)	79 (40%)
4	11 (6%)	13 (7%)
Comorbidities		
Myocardial infarction	12 (6%)	7 (4%)
Congestive heart failure	14 (7%)	11 (6%)
Coronary disease (not infarction)	27 (14%)	19 (10%)
Hypertension	87 (44%)	85 (43%)
Atrial fibrillation	25 (13%)	29 (15%)
Peripheral vascular disease	14 (7%)	9 (5%)
Cerebrovascular disease	14 (7%)	10 (5%)
Hemiplegia	1 (1%)	1 (1%)
Dementia	1 (1%)	3 (2%)
COPD or asthma	33 (17%)	28 (14%)
Connective tissue disease	7 (4%)	5 (3%)
Liver disease		
Mild	2 (1%)	3 (2%)
Moderate or severe	2 (1%)	1 (1%)
Diabetes		
Without complications	33 (17%)	42 (21%)
With complications	5 (3%)	1 (1%)
Kidney disease (moderate or severe)	7 (4%)	8 (4%)
Cancer	145 (74%)	136 (68%)
Metastatic malignancy	8 (4%)	20 (10%)
No comorbidities	21 (11%)	22 (11%)
Charlson Comorbidity Index		
Mild (0–2)	117 (60%)	119 (60%)
Moderate (3–4)	52 (27%)	51 (26%)
Severe (≥5)	27 (14%)	30 (15%)
Mean score	2·5 (1·8)	2·7 (2·1)
Medication		
Aspirin	29 (15%)	31 (16%)
Clopidogrel	9 (5%)	4 (2%)
Varfarin	15 (8%)	20 (10%)
Low molecular weight heparin	9 (5%)	4 (2%)
Direct oral anticoagulant	7 (4%)	4 (2%)
Two or more medications that affect thrombosis (anticoagulant or antithrombotic)	2 (1%)	4 (2%)
Corticosteroid or immunosuppressive medication	8 (4%)	6 (3%)
No high-risk medication	117 (60%)	127 (64%)

(Table 1 continues on next page)

further approved by the local ethics committee of Helsinki University Hospital and by each participating centre's institutional review board (Helsinki University Hospital, Oulu University Hospital, Central Finland Central Hospital, and Seinäjoki Central Hospital).

Participants

Patients who were scheduled for colon resection in participating centres were eligible for inclusion. Exclusion criteria were as follows: need for emergency surgery; bowel obstruction; colonoscopy planned to be undertaken during surgery; other indications for mechanical preparation or contraindications; allergy to drugs used in the trial (polyethylene glycol, neomycin, metronidazole); and age younger than 18 years or older than 95 years. No restrictions were applied on indication for colon resection. Both benign and malignant indications were eligible, as were both laparoscopic and open procedures. Patients provided written informed consent.

Randomisation and masking

Patients were randomly allocated in a 1:1 ratio to either MOABP or NBP. The randomisation sequence was generated using a web-based service. A block randomisation with randomly varying block size (four, six, and eight) was stratified according to centre. The web-based randomisation sequence was concealed in opaque numbered envelopes, which were opened in numerical order.

The recruiters, treating physicians, operating surgeons, data collectors, analysts, and patients were unaware of the randomisation sequence. After patients who met inclusion and exclusion criteria gave consent, the study nurse enrolled the patients to the trial, took them to another room, opened the numbered opaque envelope containing the allocated group, and instructed the patients according to the allocation group to either prepare the bowel, or not prepare the bowel. The study nurse also gave the medications and substances for mechanical bowel preparation, and then had no further role in the trial. The recruiters, treating physicians, operating surgeons, data collectors, and analysts were masked to the allocated treatment. Because patients could not be masked to allocation to mechanical bowel preparation, patients were aware of their intervention. After all the data were collected, the two groups were named as A and B. Primary and secondary outcomes were analysed without knowing the group names. Full blinding was removed only after the analyses for primary and secondary outcomes were done. Incidents of ineffective blinding (eg, patient telling the treating physicians about the bowel preparation) were recorded.

Procedures

Patients allocated to MOABP were instructed by the study nurse to prepare their bowel mechanically by drinking 2 L of polyethylene glycol (Moviprep Norgine PV; Amsterdam, Netherlands) and 1 L of clear fluid before

6 pm in the evening the day before the surgery, and take 2 g of neomycin orally at 7 pm and 2 g of metronidazole orally at 11 pm in the evening the day before the surgery. A similar per oral antibiotic regimen has been used in earlier trials comparing MOABP with mechanical bowel preparation.[25,26] Patients allocated to NBP were instructed to not prepare the bowel. The receipt of the allocated intervention was controlled by a nurse asking the patients on the morning of the surgery whether they had acted as instructed by the allocation. This information was also concealed from treating physicians and surgeons, data collectors, and data analysts, until the primary and secondary outcomes were analysed. All patients followed the ERAS protocol.[27] Prophylactic intravenous antibiotics (cefuroxime 1500 mg and metronidazole 500 mg) were given to all patients at the start of anaesthesia before skin incision. The prophylactic intravenous antibiotics were re-administered if the surgery lasted longer than 3 h from the first antibiotic dose, or if blood loss exceeded 1·5 L. Surgical skin preparation involved shaving the hair from the operation area in the morning of the operation day. Just before skin incision, the area was then washed three times with denatured 80% alcohol and left to dry.

The patients were contacted 30 days after the operation either by visit to the outpatient clinic or by phone, and at 6 months by a follow-up visit at the outpatient clinic. Patients were asked about any complications that had occurred after discharge, and clinical examination was carried out during visits to the outpatient clinic.

Outcomes

The primary outcome was SSI within 30 days after surgery. SSI was defined using Center for Disease Control and Prevention criteria[28] and was subcategorised as superficial incisional SSI, deep incisional SSI, or organ space SSI. Secondary outcome measures were Comprehensive Complication Index (CCI) score within 30 days after surgery, in which all the complications were recorded by Clavien-Dindo (CD) classification, weighted (CD 1=300, CD2=1750, CD3a=2750, CD3b=4550, CD4a=7200, CD4b=8550) and summed together (CCI=Ö(wC1+wC2…+wCx) / 2, death equals CCI=100);[26] anastomotic dehiscence within 30 days after surgery, including (1) anastomotic dehiscence detected endoscopically or radiologically, but requiring no therapeutic intervention, (2) dehiscence requiring therapeutic intervention, but no laparotomy, and (3) dehiscence requiring re-laparotomy;[29] reoperation within 30 days after surgery; readmission within 30 days after surgery; length of hospital stay (assessed at the time of discharge); mortality within 30 days and 90 days after surgery; adverse effects of antibiotics (diarrhoea, clostridium) within 30 days after surgery; and prevalence of adjuvant therapy (number of patients receiving adjuvant therapy divided by number of patients needing adjuvant therapy) assessed at 6 months after surgery.

	Mechanical and oral antibiotic bowel preparation (n=196)	No bowel preparation (n=200)
(Continued from previous page)		
Previous operations		
Previous abdominal or inguinal operation	96 (49%)	102 (51%)

Data are n (%), n/N (%), median (IQR), or mean (SD). ASA=American Association of Anesthesiologists. COPD=chronic obstructive pulmonary disorder. Patients with missing data for each variable were not included in calculations. *Two patients had missing data. †Seven patients had missing data. ‡Nine patients had missing data. §Six patients had missing data. ¶Nine patients had missing data.

Table 1: **Baseline characteristics**

	Mechanical and oral antibiotic bowel preparation (n=196)	No bowel preparation (n=200)
Indication for surgery		
Colorectal cancer	152 (78%)	153 (77%)
Colorectal adenoma or other benign tumours	19 (10%)	19 (10%)
Diverticulosis	23 (12%)	28 (14%)
Previous volvulus	2 (1%)	0
Resection site		
Right side	108 (55%)	113 (57%)
Left side	82 (42%)	80 (40%)
Colectomy	6 (3%)	7 (4%)
Resection type		
Ileocecal	3 (2%)	2 (1%)
Right hemicolectomy	103 (53%)	109 (55%)
Transverse colon resection	5 (3%)	1 (1%)
Left hemicolectomy	38 (19%)	38 (19%)
Sigmoid resection	37 (19%)	35 (18%)
Anterior rectal resection	4 (2%)	6 (3%)
Subtotal colectomy	6 (3%)	7 (4%)
Other	0	2 (1%)*
Surgical approach		
Open	26 (13%)	24 (12%)
Laparoscopic	151 (77%)	159 (80%)
Laparoscopy converted to open	19 (10%)	17 (9%)
Operation details		
Preoperative intravenous antibiotic time, min before incision	43·0 (22·9)†	42·1 (27·4)‡
Duration of operation, min	162·7 (61·8)§	159·7 (52·9)
Intraoperative blood loss, mL	121·2 (185·2)¶	116·1 (121·5)‖

No significant differences were identified between the treatment groups in any operative variables. Data are n (%), or mean (SD). Patients with missing data for each variable were not included in calculations. *One cecal resection and one reversal of Hartmann's procedure. †Three patients had missing data. ‡Two patients had missing data. §One patient had missing data. ¶Two patients had missing data. ‖One patient had missing data.

Table 2: **Operative details**

Outcome measures were assessed during the hospital stay and at 1-month clinical follow-up visit at the outpatient clinic. A regular colorectal cancer follow-up was scheduled for patients with colorectal cancer. 90-day

mortality was assessed during these follow-up visits, or, if no visits took place, directly from electronic patient records, which automatically update from the Population Register Centre.

For more on **Population Register Centre** see https://vrk.fi/en/frontpage

Tertiary outcomes were 5-year overall survival, 5-year disease-specific survival, and 5-year recurrence-free survival, and applied only to patients with cancer. These outcomes will be reported when 5-year follow-up data are available. Data were collected by using paper case report forms.

Statistical analysis

Retrospective studies have shown that the prevalence of SSIs varied from 3·2% to 8·6% in patients undergoing MOABP and from 9·0% to 16·8% in patients with NBP.[9–12] On the basis of these figures, we aimed to show an 8% absolute difference in occurrence of SSIs, and estimated that SSIs would occur in 5% of patients undergoing MOABP, and 13% of patients with NBP. With a power of 80% and significance at 5%, 396 patients would be needed to show this difference. The sample size was adjusted for a possible 5% loss, yielding a final sample size of 415 patients.

See **Online** for appendix

Categorical variables (SSI, anastomotic dehiscence, reoperation, readmission, adverse effect of antibiotics, given adjuvants) were compared using χ^2 test, or Fisher's exact test if expected cases in one cell were fewer than five. Effect size for categorical variables was estimated using odds ratios (ORs) with 95% CIs. For instances in which zeros caused problems with computation of the OR, 0·5 was added to all values. Continuous variables with normal distribution (mean CCI, mean length of hospital stay) are reported as means with SD and were compared using Student's *t* test. Effect size for such variables was estimated by reporting difference of means with 95% CIs. Continuous variables with non-normal distribution are reported as medians with IQRs and compared using the Mann–Whitney *U* test.

Statistical analyses were performed using SPSS Statistics 25 software. Statistical significance was set at a two-sided α of 0·05. Patients with missing values were excluded from analyses of that particular variable, and missing values were not imputed. Number of patients with missing values, if any, are stated within the tables or in the text when reporting the variable. Outcomes were analysed using the modified intention-to-treat principle, which included all patients who were randomly allocated to and underwent elective colon resection with an anastomosis (patients who were not operated on, those who were operated emergently while waiting for scheduled elective operation in whom anastomosis was not done, or those who underwent only explorative laparoscopy or laparotomy were excluded for all analyses). Patients who withdrew consent were analysed up to the point of withdrawal. No changes in the study protocol occurred after the trial started. The trial is registered with ClinicalTrials.gov (NCT02652637) and EudraCT (2015–004559–38).

	Mechanical and oral antibiotic bowel preparation (n=196)	No bowel preparation (n=200)	Effect size (95% CI) or mean difference (95% CI)*	p value
Surgical site infection†	13 (7%)	21 (11%)	1·65 (0·80 to 3·40)	0·17
Superficial	1 (1%)	5 (3%)	..	..
Deep	3 (2%)	4 (2%)	..	..
Organ site infection	9 (5%)	12 (6%)	..	..
Mean Comprehensive Complication Index	10·0 (13·2)	9·0 (15·5)	1·08 (–1·77 to 3·93)	0·46
Anastomotic dehiscence	7 (4%)	8 (4%)	1·13 (0·40 to 3·16)	0·82
Reoperation	16 (8%)	13 (7%)	0·78 (0·37 to 1·67)	0·53
Readmission	12/193 (6%)‡	13/196 (7%)§	1·07 (0·47 to 2·40)	0·88
Mean length of hospital stay, days	5·4 (4·7)	5·3 (4·4)	0·07 (–0·83 to 0·97)	0·87
Mortality at 30 days	0	2 (1%)	4·95 (0·24 to 103·77)	0·50
Mortality at 90 days	0	2 (1%)	4·95 (0·24 to 103·77)	0·50
Adverse effect of antibiotics	12 (6%)	13 (7%)	1·07 (0·47 to 2·40)	0·88
Diarrhoea	10 (5%)	11 (6%)	..	..
Clostridium spp infection	0	1 (1%)	..	..
Allergic reaction	0	1 (1%)	..	..
Candida spp infection	2 (1%)	0	..	..
Adjuvant treatment given (out of number who needed treatment)	60/72 (83%)	74/87 (85%)	0·88 (0·37 to 2·07)	0·77

Data are n (%), n/N (%), or mean (SD) unless otherwise specified. Patients with missing data for each variable were not included in calculations. *For means, difference is given with 95% CI; for binary outcomes, odds ratio is given with 95% CI. †Only the most severe type of surgical site infection is reported here; table 4 contains a complete list of all complications (including multiple types of surgical site infections). ‡Three patients had missing data. §Four patients had missing data.

Table 3: **Primary and secondary outcomes**

Role of the funding source

The funders of the study had no role in the study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author (LK) had full access to all the data in the study. LK and VS had final responsibility for the decision to submit for publication.

Results

Between March 17, 2016, and Aug 20, 2018, 736 patients were assessed for eligibility in four Finnish hospitals (figure; appendix). 229 patients met an exclusion criterion, 86 declined to participate, and four patients were participating in other trials. 417 patients were enrolled and randomly allocated to treatment. Of the randomised patients, 21 were excluded from the analyses after randomisation, leaving 396 patients in the final modified intention-to-treat analyses (196 patients for MOABP *vs* 200 patients for NBP).

Patient baseline characteristics were similar between the two groups (table 1), as were perioperative details (table 2). Preoperative prophylactic intravenous antibiotic times were similar in both groups (table 2). The operation time was 180–240 min in 81 patients (37 in the MOABP group and 44 in the NBP group), and 47 (24 in the MOABP

group and 23 in the NBP group) of these 81 patients were given another dose of prophylactic intravenous antibiotics. The operation time exceeded 240 minutes in 37 patients (21 in the MOABP group and 16 in the NBP group), and 15 (nine in the MOABP group and six in the NBP group) of these 37 patients were given another dose of prophylactic intravenous antibiotics. Blood loss did not exceed 1·5 L in any of the patients. Masking was reported to have been unsuccessful in one patient in the MOABP group and none in the NBP group.

SSI was detected in 13 (7%) of 196 patients in the MOABP group and in 21 (11%) of 200 in the NBP group (OR 1·65 [95% CI 0·80 to 3·40], p=0·17; absolute difference 3·9% [95% CI –1·6 to 9·4]; table 3). The subgroups of SSIs were similarly distributed in both groups (table 3). CCI was similar between the groups (table 3), and anastomotic dehiscence was detected in seven (4%, all Class C) of patients in the MOABP group versus eight patients (4%, one Class A, seven Class C) in the NBP group (table 3). Reoperation was required in 16 (8%) patients in the MOABP group versus 13 (7%) patients in the NBP group (table 3). Reoperation was because of anastomotic dehiscence in seven patients, suspected anastomotic dehiscence in two patients, fascial rupture in three patients, occlusion in one patient, intra-abdominal bleeding in two patients, and ureter lesion in one patient in the MOABP group; and because of anastomotic leakage in seven patients, intra-abdominal bleeding in one patient, fascial rupture in three patients, occlusion in one patient, and intestinal necrosis in one patient in the NBP group. 12 (6%) patients were readmitted to hospital in the MOABP group because of abdominal pain (three patients), SSI (one patient), ileus (three patients), intraluminal bleeding (one patient), fever (one patient), and urinary tract infection and retention (three patients). 13 (7%) patients were readmitted to hospital in the NBP group for abdominal pain (three patients), SSI (five patients), ileus (two patients), intraluminal bleeding (two patients), and diarrhoea (one patient). One patient in both groups was still in hospital after 30 postoperative days. Mean length of hospital stay was similar in both groups (table 3). There were no deaths within 90 days in the MOABP group. Two patients died within 90 days in the NBP group (both within 30 days). One of them (age 83 years, American Association of Anestheologists [ASA] class 4, Charlson Comorbidity Index 6) was vomiting and died of post-operative pneumonia; the other (age 82 years, ASA class 3, Charlson comorbidity index 4) had extensive postoperative intra-abdominal bleeding, underwent two relaparotomies because of bleeding, and died from postoperative myocardial infarction and stroke. The potential adverse effects of antibiotics (diarrhoea, *Clostridium difficile* infections, or allergic reactions) were similar between the two groups (table 3). Of the patients needing adjuvant therapy, 60 (83%) of 72 patients in the MOABP group and 74 (85%) of 87 in the NBP group actually received adjuvant therapy (table 3). We summarise adverse effects and

	Mechanical and oral antibiotic bowel preparation (n=196)	No bowel preparation (n=200)
No postoperative complications	103 (53%)	116 (58%)
Grade 1 complications (one or more per patient)	53 (27%)	54 (27%)
Superficial wound infection, wound dehiscence*	2 (1%)	6 (3%)
Ileus (vomiting, nasogastric tube placement)	37 (19%)	32 (16%)
Electrolyte imbalance	6 (3%)	6 (3%)
Collapse	3 (2%)	0
Urinary retention	3 (2%)	5 (3%)
Haematuria	1 (1%)	0
Urinary tract stone	1 (1%)	0
Diarrhoea	10 (5%)	11 (6%)
Incisional site bleeding	1 (1%)	1 (1%)
Bleeding ex ano, no need for any therapy	0	2 (1%)
Abnormal intensive incisional or operation site pain	2 (1%)	1 (1%)
Fever	0	2 (1%)
Thrombopenia	0	1 (1%)
Delirium	1 (1%)	0
Shortness of breath	1 (1%)	2
Headache	1 (1%)	0
Diuretics	1 (1%)	0
Grade 2 complications (one or more per patient)	47 (24%)	35 (18%)
Prolonged ileus with medication	8 (4%)	6 (3%)
Allergic reaction	0	1 (1%)
Fever with administrated antibiotics	10 (5%)	7 (4%)
Antibiotics administrated, reason not known	3 (2%)	3 (2%)
Pneumonia	5 (3%)	3 (2%)
Diarrhoea with *Clostridium difficile*	0	1 (1%)
Pulmonary embolism	3 (2%)	2 (1%)
Deep vein thrombosis	1 (1%)	0
Urinary tract infection	5 (3%)	0
Congestive heart failure worsening	2 (1%)	2 (1%)
Atrial fibrillation	4 (2%)	3 (2%)
Abscess	0	3 (2%)
Postoperative bleeding or anaemia, transfusion	9 (5%)	13 (7%)
Intraluminal haemorrhage, transfusion	1 (1%)	0
Incisional site pain, local anaesthetic injection	0	1 (1%)
Anastomotic dehiscence, class A, no intervention	0	1 (1%)
Ascites	0	1 (1%)
Candida spp infection	2 (1%)	0
Grade 3a complications (one or more per patient)	6 (3%)	3 (2%)
Intraluminal stricture, endoscopic treatment	1 (1%)	0
Intraluminal haemorrhage, endoscopic treatment	2 (1%)	0
Intra-abdominal abscess with percutaneous drainage	0	2 (1%)
Pleural effusion, pleural drainage	4 (2%)	1 (1%)
Ureteral lesion, catheter and irrigation	1 (1%)	0
Grade 3b (one or more per patient)	16 (8%)	10 (5%)
Anastomotic dehiscence, laparotomy	6 (3%)	5 (3%)
Abscess, postoperative peritonitis, laparotomy	2 (1%)	0
Intra-abdominal bleeding, laparotomy	2 (1%)	0
Intraluminal bleeding, endoscopy, general anaesthesia	1 (1%)	1 (1%)
Fascial dehiscence, resuture, general anaesthesia	4 (2%)	3 (2%)

(Table 4 continues on next page)

	Mechanical and oral antibiotic bowel preparation (n=196)	No bowel preparation (n=200)
(Continued from previous page)		
Ureter lesion, laparotomy	1 (1%)	0
Intestinal occlusion, laparotomy	1 (1%)	1 (1%)
Grade 4a complications	0	0
Grade 4b complications (one or more per patient)	1 (1%)	3 (2%)
Anastomotic dehiscence leading to multiple organ dysfunction and intensive care	1 (1%)	2 (1%)
Necrosis of bowel proximal to anastomotic site leading to multiple organ dysfunction and intensive care	0	1 (1%)
Grade 5 complications (death)	0	2 (1%)
Postoperative intra-abdominal bleeding, stroke	0	1 (1%)
Pneumonia	0	1 (1%)

*Only the most severe surgical site infection is reported in table 3, whereas all cumulative and multiple complications are reported in this table; for this reason, these values differ between the tables. Individual patients might have several complications reported.

Table 4: **Cumulative postoperative complications within 30 days classified by use of Clavien-Dindo grade**

complications in table 4. Almost half of the patients experienced a complication, of which most were minor (CD grade 1 or 2). The most common complication was ileus, which was treated conservatively.

Discussion

To our knowledge, this trial was the first prospective randomised trial comparing MOABP with NBP before elective colon resection. The development of SSI was similar in patients undergoing MOABP to those with NBP (13 [7%] of 196 *vs* 21 [11%] of 200). Cumulative postoperative complications, as measured by the highly sensitive CCI,[30] did not indicate any difference in overall postoperative morbidity. These results suggest that MOABP is ineffective in reducing SSIs or overall morbidity of colon surgery compared with NBP.

Several large retrospective series have reported that SSI occurs in 3·2–8·6% of patients undergoing MOABP and 9·0–16·8% of patients receiving NBP.[9–13,15,31] Most of these series used data from ASC NSQIP and probably consisted of (at least partially) the same patients.[9–13,16,31] The absolute (percentage point) difference in SSIs between MOABP and NBP in these series have varied between 4·7% and 10·0%. In most of these series, the laparoscopic approach was used in 61–71% of patients,[10,11,31] which is slightly lower than our use of laparoscopic surgery (78%), and could affect the development of SSIs. A European prospective non-randomised multicentre cohort from the 2017 European Society of Coloproctology[32] collaborating group showed a lower risk of anastomotic leak in patients undergoing MOABP than in those receiving NBP. However, this cohort included only left-sided colectomies and included rectal resections. We found a 4% absolute difference between MOABP and NBP, but this difference was not statistically significant. Furthermore, the retrospective series reported a marked decrease in overall 30-day morbidity in favour of MOABP.[33,34] By contrast, our study did not show that MOABP decreased overall postoperative morbidity. These between-study differences are likely to be because of several biases in these retrospective series, as emphasised by Beyer-Berjot and Slim.[35] Patients who did not undergo preoperative MOABP in these retrospective trials had more comorbidities[10,13,31] and a more advanced stage of colorectal cancer than those who had NBP.[10,11,31] Patients were classified according to the type of preparation they were intended to receive, not what they actually received.[10] The retrospective series did not report the use of preoperative prophylactic intravenous antibiotics or the types of oral antibiotics. Furthermore, sample sizes in these reports varied widely, although they consisted of patients from the same database from the same time period,[11,13,31] which might indicate the presence of selective reporting. The differences might also be because of different scoring systems for postoperative complications. We used the most comprehensive and sensitive index, CCI, to obtain reliable data for postoperative complications. This index considers all the cumulative complications instead of only recording the most severe one (which is usually the case when reporting complications using CD classification only).[30] Furthermore, we did not find any differences in the proportion of patients who had reoperations, were readmitted to hospital, or died, and the length of hospital stay was similar between the groups. Considering these secondary outcomes and the potential disadvantage of the MOABP for the patient (discomfort involved in drinking large amounts of liquid, nausea, dehydration) a small decrease in the risk of developing a superficial SSI would not be worthwhile. Notably, adverse effects of antibiotics were similar between the groups, which might be because both groups received preoperative prophylactic intravenous antibiotics. Retrospective series have also reported similar,[36] or an even lower prevalence of *C difficile* infection after MOABP.[37] Although no other randomised controlled trial comparing MOABP with NPB exists, several randomised controlled trials show beneficial results for MOABP when compared with mechanical bowel preparation only.[21–23] These results cannot be extrapolated directly to the NBP strategy, because mechanical bowel preparation could increase development of SSIs.[24] The randomised controlled trials comparing MOABP with oral antibiotic prophylaxis found no difference in terms of SSI.[20,38]

This trial has some limitations. First, it was powered to detect an 8% absolute difference in SSIs. We found a 4% absolute difference in SSIs, which did not reach statistical significance. Thus, this trial was underpowered to detect such a small difference. From a clinical point of view and from a patient's perspective, overall postoperative morbidity is more important than SSIs. Overall postoperative complications were similar and the complication index was slightly higher in the MOABP group than the NBP group. Second, this trial was not

double-blinded, but because of the nature of the intervention, such blinding would have been impossible to implement. Patients will inevitably know whether they have undergone mechanical bowel preparation or not, even if placebo bowel preparation was introduced. However, we sought to keep the allocation group concealed from all the others by all possible means, and even the results were analysed without knowing the allocation group. Third, no prespecified subgroup analyses were planned for right versus left colectomies. Fourth, we used single doses of oral antibiotics the day before the surgery. The single doses were based on the protocols of earlier trials comparing MOABP to mechanical bowel preparation,[25,26] although some other trials divided the dose into several portions administrated within 1 day or several days.[26,38] The different oral antibiotic regimens might influence the effectiveness of the antibiotics, but an earlier randomised trial comparing a single dose with three doses did not show a difference in terms of reducing SSI, but a single dose was better tolerated by the patients than was three doses.[26] Finally, the decision to use CT scans to detect anastomotic dehiscence was made on the basis of clinical signs and symptoms. No routine radiographic studies were included in the protocol to detect asymptomatic anastomotic leaks. However, we do not do imaging studies routinely in asymptomatic patients in our normal daily clinical practice, and clinical significance of such asymptomatic, but radiographic anastomotic leak after colon surgery is unclear.

This trial has several strengths. First, this was a multicentre trial including both university and non-university hospitals, thus improving its external validity. Second, the patients were on average aged 70 years, and approximately 50% were patients at high-risk according to their ASA class 3–4, indicating that the case-mix accurately represents daily clinical practice. Finally, postoperative morbidity was meticulously recorded and reported by use of the most sensitive and accurate complication scoring system available.

To our knowledge, this is the first prospective, randomised, controlled trial comparing MOABP with no preparation. Another trial (COLONPREP; NCT03475680) will be recruiting to compare MOABP with NBP using the same antibiotics, in colonic surgery.

In summary, our results suggest that MOABP does not reduce the occurrence of SSIs or overall morbidity after colonic surgery.

Contributors

LK and VS devised the concept of the study. LK, TL, SK, TS, and VS designed the study. LK, TL, SK, SR, KK, AE, TP, and TS participated in acquisition of data. LK and VS analysed and interpreted the data. LK and VS wrote the initial draft. All authors critically revised the manuscript and approved the final version.

Declaration of interests

VS reports grants from Vatsatautien Tutkimussäätiö Foundation, Mary and Georg Ehrnrooth's Foundation, and Helsinki University Hospital research funds, during the conduct of the study; grants from Finnish Surgical Society, Finska Läkaresällskapet, and Finnish Gastroenterological Society; personal fees from City of Vantaa, Finnish Gastroenterological Society, Novartis, and University of Helsinki; and non-financial support from Astellas, outside of the submitted work. TS reports personal fees from Johnson & Johnson's laparoscopic colorectal surgery advisory board, outside of the submitted work. All other authors declare no competing interests.

Data sharing

The collected data or related documents will not be made available to others.

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